

PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<p>(51) International Patent Classification 6 : A61F 2/06</p>	<p>A1</p>	<p>(11) International Publication Number: WO 97/04721 (43) International Publication Date: 13 February 1997 (13.02.97)</p>
<p>(21) International Application Number: PCT/CA96/00504 (22) International Filing Date: 25 July 1996 (25.07.96) (30) Priority Data: 9515282.3 25 July 1995 (25.07.95) GB 9605486.1 15 March 1996 (15.03.96) GB (71) Applicant: MEDSTENT INC. [CA/CA]; Unit 5, 91 Kelfield Road, Rexdale, Ontario M9W 5A3 (CA). (72) Inventors: LEE, Michael, J.; 324 Purcell Cove Road, Halifax, Nova Scotia B3P 1C7 (CA). CREWE, Katherine, H.; 42 Lake Crescent, Etobicoke, Ontario M8V 1V8 (CA). MASTRANGELO, Christine; 1 Place Pier Court #1012, Etobicoke, Ontario M8V 3W9 (CA). (74) Agent: ORANGE, John, R., S.; Orange and Associates, Toronto Dominion Bank Tower, Toronto-Dominion Centre, Suite 3600, P.O. Box 190, Toronto, Ontario M5K 1H6 (CA).</p>		<p>(81) Designated States: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, ARIPO patent (KE, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).</p> <p>Published With international search report.</p>
<p>(54) Title: EXPANDIBLE STENT</p> <div data-bbox="438 1134 1266 1659"><p>The diagram illustrates a cross-section of an expandible stent. It features a central tubular body composed of multiple longitudinal struts. These struts are interconnected by multi-bar linkages, which are shown as horizontal bars with notches or tabs that fit into the struts. The struts are labeled 12, and the linkages are labeled 14. The entire assembly is labeled 10. Arrows 2 point to the ends of the stent, and arrow 16 points to the struts.</p></div> <p>(57) Abstract</p> <p>A stent has a tubular body with longitudinal struts interconnected by multi-bar linkages. The struts inhibit foreshortening of the body and relative rotation between the links in the linkages permits radial expansion. The links are plastically deformed as they are expanded to maintain the expanded diameter.</p>		

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AM	Armenia	GB	United Kingdom	MW	Malawi
AT	Austria	GE	Georgia	MX	Mexico
AU	Australia	GN	Guinea	NE	Niger
BB	Barbados	GR	Greece	NL	Netherlands
BE	Belgium	HU	Hungary	NO	Norway
BF	Burkina Faso	IE	Ireland	NZ	New Zealand
BG	Bulgaria	IT	Italy	PL	Poland
BJ	Benin	JP	Japan	PT	Portugal
BR	Brazil	KE	Kenya	RO	Romania
BY	Belarus	KG	Kyrgyzstan	RU	Russian Federation
CA	Canada	KP	Democratic People's Republic of Korea	SD	Sudan
CF	Central African Republic	KR	Republic of Korea	SE	Sweden
CG	Congo	KZ	Kazakhstan	SG	Singapore
CH	Switzerland	LJ	Liechtenstein	SI	Slovenia
CI	Côte d'Ivoire	LK	Sri Lanka	SK	Slovakia
CM	Cameroon	LR	Liberia	SN	Senegal
CN	China	LT	Lithuania	SZ	Swaziland
CS	Czechoslovakia	LU	Luxembourg	TD	Chad
CZ	Czech Republic	LV	Latvia	TG	Togo
DE	Germany	MC	Monaco	TJ	Tajikistan
DK	Denmark	MD	Republic of Moldova	TT	Trinidad and Tobago
EE	Estonia	MG	Madagascar	UA	Ukraine
ES	Spain	ML	Mali	UG	Uganda
FI	Finland	MN	Mongolia	US	United States of America
FR	France	MR	Mauritania	UZ	Uzbekistan
GA	Gabon			VN	Viet Nam

EXPANDIBLE STENT

Expandable stents are widely used to provide local reinforcement in fluid-carrying vessels within the human body. The stent is essentially a cylindrical member which may be expanded radially to dilate the vessel and to provide support for the wall of the vessel to maintain it in the dilated condition.

In order to insert the stent, it has previously been proposed to place the stent into the vessel on an expandable or balloon catheter. With the stent positioned at the appropriate location, the catheter is inflated and the stent is caused to expand radially against the wall of the vessel. Once the stent is expanded to the required diameter, the catheter is deflated and may be removed, leaving the stent in position.

The stent must of course remain expanded against the wall of the vessel and should be capable of withstanding the forces imposed by the wall of the vessel. Moreover, the stent should be able to negotiate tight turns in the arterial system during placement while minimizing damage to the arterial wall.

A number of different mechanisms have been proposed to permit the expansion of the stent, including devices which reorient the components forming the stent so that they may adopt a greater overall diameter.

In another class of stents, as typified by the stent shown in USP 4,733,665 to Palmaz, the stent is configured to be plastically deformable so that after expansion it retains the increased diameter. In the Palmaz stent, the plastic deformation is provided by means of an open-mesh diamond structure. As the catheter is expanded, the intersecting members of the mesh deform so that the stent adopts an increased diameter.

With the arrangements shown in the Palmaz stent and similar configurations, a radial expansion of the stent is accompanied by an axial foreshortening of the stent. The degree of foreshortening is predictable but

the ultimate location of the stent along the vessel is not predictable. Thus, one end of the stent may remain stationary relative to the blood vessel so that the opposite end is subjected to the maximum axial displacement or there may be progressive foreshortening from both ends with an intermediate location remaining stationary. The foreshortening of the stent leads to an unpredictable location for the stent in its expanded condition and induces relative movement in an axial direction between the vessel wall and the stent which is generally undesirable.

It is therefore an object of the present invention to provide a stent in which the above disadvantages are obviated or mitigated.

In general terms, the present invention provides a stent in which a plurality of circumferentially-spaced longitudinal struts are interconnected by multi-bar linkages. Adjacent links of the linkages are angularly disposed to one another such that a radial force causes relative rotation between adjacent links to permit radial enlargement of the stent.

The longitudinal struts inhibit foreshortening of the stent so that the final location of the stent can be predicted.

Embodiments of the invention will now be described by way of example only with reference to the accompanying drawings, in which

Figure 1 is a side elevation of an assembled stent;

Figure 2 is a view on the line 2-2 of Figure 1;
Figure 3 is a developed view of the stent shown in Figure 1;

Figure 4 is a view on an enlarged scale of a portion of the stent shown in Figures 1-3;

Figure 5 is a view of the portion of the stent shown in Figure 4 after radial expansion;

Figure 6 is a view similar to Figure 4 of an

alternative embodiment of stent;

Figure 7 is a view of the embodiment of Figure 6 after radial expansion;

5 Figure 8 is a further alternative of stent shown in Figure 4;

Figure 9 is a view of the embodiment of Figure 8 after radial expansion;

Figure 10 is a comparative curve between the embodiments of stent shown in Figures 4, 6 and 8;

10 Figure 11 is a perspective view of a further embodiment of stent;

Figure 12 is a developed view of the embodiment of stent shown in Figure 11;

15 Figure 13 is an enlarged view of a portion of the stent shown in Figure 11;

Figure 14 is a view similar to Figure 9 showing the stent after radial expansion;

Figure 15 is a sectional view of a stent support and catheter; and

20 Figure 16 is a developed view, similar to Figure 12, of a further embodiment.

Referring therefore to Figure 1, a stent 10 has a generally tubular body 12 which is initially dimensioned to permit insertion into a vessel such as an artery. The body 12 includes a plurality of longitudinal struts 14 which are interconnected by multi-bar linkages 16. The linkages 16 are regularly spaced along the axial extent of the struts 14 and maintain struts 14 in circumferentially spaced relationship.

30 As can best be seen in Figure 4, each of the linkages 16 includes a pair of oppositely directed circumferential links 18 with axial links 20 connected to the circumferential links 18 and extending parallel to the struts 14 but spaced therefrom. The axial links 20 are connected to an L-shaped corner link 22 which has an axial leg 24 and circumferential leg 26. The legs 26 of
35 opposed corner links 22 are interconnected by a

circumferential connecting link 28 to interconnect the adjacent struts 14. The links 18,20,22 and 28 of the linkage 16 are formed by removal of material from a seamless tube of bio-compatible material so that the links are integrally connected to one another. Typically such material would be a metal such as both pure and alloyed titanium, platinum, nitinol memory metals, gold or stainless steel, and the linkage may suitably be machined through micro machining techniques. Other materials could be used that are considered suitable for implantation including plastics materials having the requisite properties.

Each of the linkages 16 is similar and the relative dimensions between the links in each linkage determine the change in diameter for a given load. In a typical example, as shown in Figure 4, taking the length of the connecting link 28 to be of unit length, then the relative dimensions of the other links as indicated by the letters on Figure 4 are as follows:

a	b	c	d	e	f	g	h	i	j	k
1	2	1	0.625	1.125	0.125	2.125	2.0	1.375	1.125	0.125

The stent 10 is typically inserted into the vessel by using a balloon catheter 60. The stent 10 is mounted on the catheter 60 shown in Figure 15. To assist in placement of the stent 10 on the catheter 60, the stent is initially located on a support 62 that has a bar-like head 64 and a tapered body 66. The stent 10 is snugly received on the body 66 which has a concave recess 68 at one end to locate the tip of catheter 60. A bore 70 extends through the body 66 to accommodate a wire if the catheter is of the type that employs such.

A protective sleeve 72 is located over the body

66 and is retained on a boss 74 on the head 64. The sleeve 72 thus protects the stent 10 from extraneous external forces with the body 66 providing support for the stent 10 in transit.

5 To transfer the stent to the catheter 60, the sleeve 72 is removed and the body 66 is aligned with the catheter 60. The stent may then be slid axially from the body 66 over the catheter 60 and the support and sleeve discarded. In this way, the stent is guided during
10 transfer and the placement of the stent on the catheter facilitated.

The recess 68 assists in locating and aligning the catheter 60 during transfer and of course the wire, if present, may be fed through the bore 70.

15 The stent 10 is located on the body 66 such that the links 28 are closer to the boss 74 than the associated links 18. Transfer of the stent 10 to the catheter thus ensures that the stent 10 is oriented on the catheter 60 such that the connecting link 28 of the
20 linkage 16 is in advance of the circumferential links 18 during insertion of the stent 10 into the vessel.

The catheter is inserted into the vessel in a conventional manner until it is located at the stenosis.

25 After placement within the vessel, the catheter is then inflated to apply a radially expanding force to the stent.

As shown in Figure 5, the application of the radial force causes the circumferential spacing of struts 14 to increase. The circumferential links 18 are carried
30 with the struts 14 and a hinging action occurs at the connection of the axial link 20 to both the circumferential link 18 and the corner link 22 by plastic deformation of the links. Similarly, the connecting link 28 hinges at its connection to the corner link 22 to
35 provide a hinging action between the links. The links 22 is thus bodily rotated as the struts 14 are spread.

By virtue of the relatively narrow links 20,22,

the hinging at their junction to the larger links 18,22 exceeds the yield point of the material and causes a permanent deformation and increase in diameter. A pair of spaced hinge points is thus established and thus the
5 total rotation required between the axial links 20 and circumferential link 28 is distributed between two locations.

The catheter is then deflated and removed, leaving the stent 10 in situ. It will be noted, however,
10 that during inflation the struts 14 maintain the axial spacing between the circumferential links 18 so that the overall length of the stent remains the same with no relative axial movement between the vessel and the stent.

In tests with samples of the configuration of
15 Figures 4 and 5, an extension from the spacing of the struts 14 was increased from an initial value of 6 units to 8.48 units upon application of loads consistent with those used in the expansion of such stents.

An alternative embodiment of linkage 16 is
20 shown in Figures 6 and 7, in which like components will be denoted with like reference numerals with a suffix 'a' added for clarity.

In the embodiment of Figure 6, the circumferential link 18a is formed as a pair of
25 rectangular nodes 30,32 interconnected by a narrow bar 34. The length of the axial link 20a is reduced to .5 of a unit value and a corresponding reduction in the length of the connecting link 28 to 0.5 is made. As may be seen in Figure 7, the application of the radial load causes
30 the connection at the bar 34 to plastically deform, allowing rotation of the rectangular bar 32. The connecting link 28a is also subjected to bending load as well as plastic deformation at the connection to the links 22a.

35 In tests conducted with samples of the arrangements shown in Figures 6 and 7, the initial spacing of the struts 14 was increased to 8.5 units after

application of a radial force consistent with that found in balloon catheters.

A further embodiment is seen in Figure 8 where again like reference numerals will be used to denote like components with a suffix 'b' added for clarity. In the embodiment of Figure 8, the connection between the connecting links 20b and the circumferential links 18b progressively tapers to the dimension F. In a similar manner, the junction between the connecting link 28b and the link 22b progressively tapers and in each case the overall length of the links 20b, 28b is reduced from 1 unit value to 0.5 unit value. A tapering in the order of 45° is found to be appropriate.

The results of tests conducted on the embodiment shown in Figures 4, 6 and 8 are represented on the curve of Figure 9. This curve represents the applied radial load and the deflection obtained and it will be seen that in each embodiment there is an initial proportional increase of load and deflection followed by a much flatter curve indicating a plastic deformation. Thereafter, the load progressively increases, indicating that the orientation of the links is approaching a linear orientation. It will be seen that the embodiment of Figure 8 provides a lower load to achieve the requisite deflections. With the provision of the relatively narrow links, it is possible to control the radial force necessary to expand the stent and the location at which the bending will occur. The force necessary to achieve radial expansion must be compatible with the forces available from a balloon catheter and the reduced width of the links permits this. Moreover, the plastic deformation of the narrow links maintains control of the orientation of the wider links during expansion.

A further embodiment is shown in Figures 11-14 offering enhanced flexibility for the stent during insertion, as may be needed to negotiate tight turns in the arterial system during placement, thereby minimizing

damage to the arterial wall.

In the embodiment of Figures 11-14, each of the struts 14c is segmented so as to be comprised of either a series of unitary struts 40 or a series of linking struts 42.

The unitary struts 40 alternate with linking struts 42 about the circumference of stent 10c and in the preferred embodiment an even number of each is provided so that the linking struts 42 are diametrically opposed. It is preferred that four linking struts 42 are provided and are circumferentially spaced at 90° intervals.

Each of the unitary struts 40 extend between two of the linkages 16c so as to interconnect them. The unitary struts are spaced apart from one another by a gap indicated at 44 so that each linkage 16c is connected to only one of the adjacent linkages 16c. By contrast, the linking struts 42 extend between four of the linkages 16c and are then spaced from the next of the linking struts 42 by a space indicated at 46.

The gaps 44 between the unitary struts are circumferentially aligned to provide annular bands 48 whereas spaces 46 are staggered between alternate linking struts 42. Each of the linking struts 42 has a waist 50 to provide a region of enhanced flexibility in a plane tangential to the surface of the stent 10c. The waist 50 is aligned with one of the bands 48 and so provides the connection across the band 48 between the linkages 16c.

As can be seen in Figure 11, the waists 50 are located at diametrically opposed locations in the respective bank 48 to define a pair of pivot axes X-X. By virtue of the staggered relationship between adjacent linking struts 42, the waists 50 are displaced by 90° in adjacent bands 48 so that the pivot axes X-X are disposed at 90°.

This arrangement provides flexibility about mutually perpendicular axially spaced axes allowing

relative pivotal movement between sections of the stent to conform to the vessel into which it is inserted.

The linkage 16c is shown in detail in Figure 13 and includes circumferential links 18c and axial links 20c connected by a node 32c.

The circumferential link 28c is connected to axial link 20c by corner link 22c which is formed as a rectangular leg 24c.

It will be noted that the connection of each of the links 18c, 20c, 28c to the struts 134, nodes 32c and corner link 22c by radiused fillets 52 that reduce local stress concentrations.

In one preferred example, the relative dimensions are as follows:

a	b	c	d	e	f	g	h	i
1.20	0.75	1.40	1.40	2.00	0.90	0.25	6.9	5.30

The fillets 52 are each 0.125 and the thickness of the material between 0.0625 and 0.125.

With this configuration, the application of a radial load results in the circumferential expansion shown in Figure 14 from which it can be seen that a uniform bending of the links 18c is obtained and that the axial links 20 have assumed a circumferential orientation.

Upon circumferential expansion, the linking struts 42 inhibit foreshortening as each band 48 has two axial struts that inhibit relative axial movement between adjacent linkages 16c. At the same time the relatively flexible waists 50 disposed at 90° to one another provides the requisite flexibility for insertion of the stent 10c.

Although the embodiment of Figure 11 shows axes of rotation at 90° to one another, alternative arrangements may be used by varying the relative orientation of the waisted links. For example, by

spacing the links at 60° angles, three axes of rotation are obtained at axially spaced locations.

The following relative dimensions of linkage 16 have also been found to provide satisfactory performance:

5 Example I:

a	b	c	d	e	f	g	h	i
10	7.5	11	17.8	38.6	12.3	3	46	74.2

Example II:

10

a	b	c	d	e	f	g	h	i
10.3	7.7	12.2	17.8	38.6	12.3	3	48.2	74.2

Example III:

a	b	c	d	e	f	g	h	i
10.0	7.5	11	14.3	20.4	9.2	3	46	49

15

In each of these examples, the units are 0.001 inches and the thickness of the material used was 0.003 inches.

20

In Examples I and III, the width, ie. circumferential dimension, of the struts 14 was 5 units and the axial spacing between adjacent linkages 16 was 12 units.

In Example II, the width of the struts 14 was 2.85 units and the axial spacing between adjacent linkages was 3 units.

25

In each case, the linkages repeated 4 times about the circumference. The diameter of the stent prior to expansion was 65 units and after expansion with a 45°

rotation of the links 20c an outside diameter of 197 units was obtained with Example II and 152.3 units with Example III. The axial spacing between linkages 16 was sufficient to permit the bodily rotation of the corner
5 links as the stent expands radially. The provision of the strut 14 inhibits foreshortening and therefore ensures that the linkages can rotate as required.

A further embodiment is shown in Figure 16 in which like components will be identified with like
10 reference numerals with a suffix 'd' added for clarity. The embodiment of Figure 16 is similar to that shown in Figures 12 and 13. However, each of the struts 14d is segmented into a series of unitary struts 40d that extend between two adjacent linkages 16d. The struts 40d are
15 staggered circumferentially to alternate the direction of connection between adjacent linkages. The unitary linkages 40d are thus aligned at diametrically opposed locations and thus define a pair of orthogonal axes at axially spaced locations to provide flexibility during
20 insertion.

The stent will of course be dimensioned to fit within the intended vessel and engage the wall when extended. A typical stent for insertion in an artery will have a diameter of between 1.5 mm and 3.5 mm when
25 inserted and may have a diameter of between 2 mm and 12 mm when expanded.

We claim:

1. A stent having a generally tubular body with a plurality of circumferentially spaced longitudinal struts
5 extending parallel to a longitudinal axis of said body, circumferentially adjacent pairs of said struts being interconnected by a plurality of linkages axially spaced from one another and each including a plurality of links connected to one another, adjacent links of said linkages
10 being angularly disposed relative to one another such that a radial force causes relative rotation between adjacent links and plastic deformation thereof to permit radial expansion of said stent, said struts inhibiting relative axial movement between said linkages and
15 foreshortening of said body.

2. A stent according to claim 1 wherein each of said linkages includes a pair of circumferentially extending links and a pair of axial links connected at
20 one end to respective ones of said circumferentially extending links, opposite ends of said axial links being connected to one another by a circumferential link axially spaced from said circumferentially extending links.

25 3. A stent according to claim 2 wherein said axial links and said circumferential link are enlarged at their intersection to provide a pair of spaced hinges at each connection thereof.

30 4. A stent according to claim 2 wherein said axial links are enlarged at their intersection with said circumferentially extending links.

35 5. A stent according to claim 4 wherein each of said circumferentially extending links and said axial links are enlarged at their intersection to provide a

pair of spaced hinges at each connection thereof.

6. A stent according to claim 5 wherein said axial links and said circumferential links are enlarged at their intersection to provide a pair of spaced hinges at each connection thereof.

7. A stent according to claim 1 wherein each of said struts extends between at least two axially adjacent linkages.

8. A stent according to claim 7 wherein selected ones of said struts are interrupted periodically along said body to provide a gap between axially adjacent pairs of linkages, the axial location of said gaps being staggered about the circumference of said body whereby relative axial movement between said linkages is inhibited by a strut circumferentially spaced from and axially aligned with said gap.

9. A stent according to claim 8 wherein struts axially aligned with said gaps are reduced in section to facilitate flexure thereof.

10. A stent according to claim 9 wherein struts having a reduced section are diametrically aligned to provide an axis of relative pivotal movement between said adjacent linkages.

11. A stent according to claim 10 wherein a plurality of gaps are provided at axially spaced locations and struts having a reduced section are diametrically aligned at each location to define respective pivot axes.

12. A stent according to claim 11 wherein said pivot axes are angularly disposed relative to one

another.

13. A stent according to claim 12 wherein said axes are disposed at 90° to one another.

5

14. A stent according to claim 1 wherein said links are perpendicular to one another.

15. A stent according to claim 10 wherein said
10 links are enlarged at their intersection.

16. A stent according to claim 15 where enlargements of said links are generally rectangular.

1/14

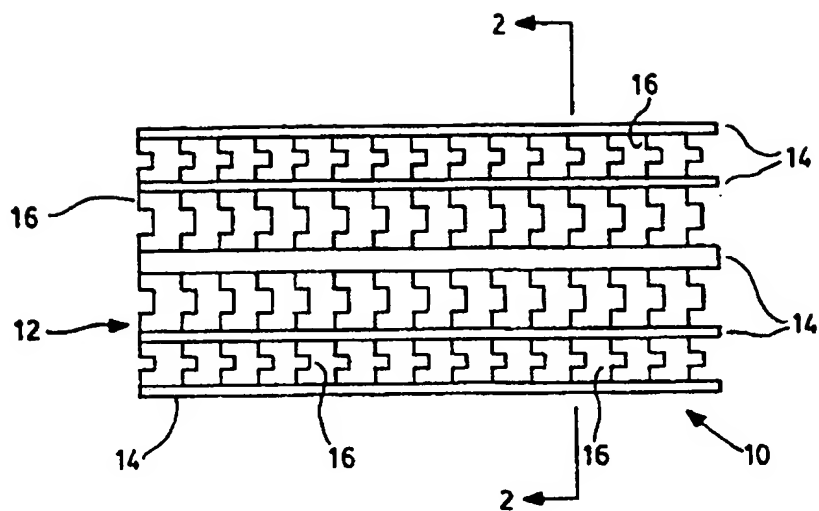


FIG. 1

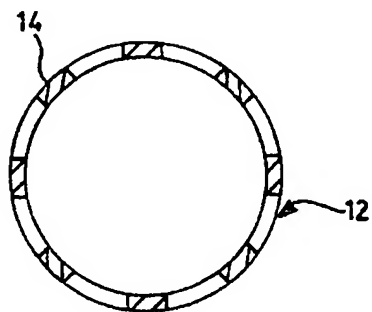


FIG. 2

2/14

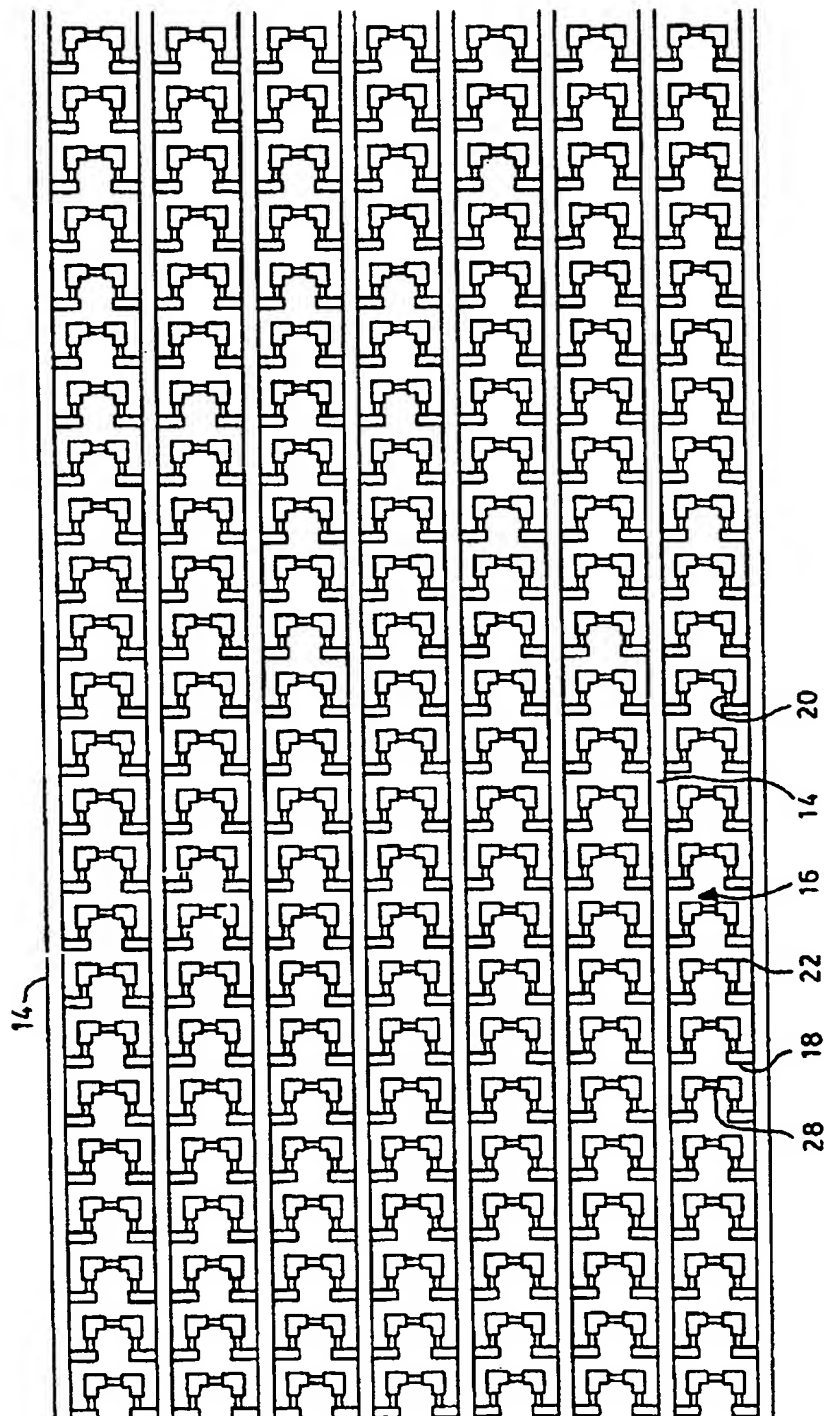


FIG. 3

3/14

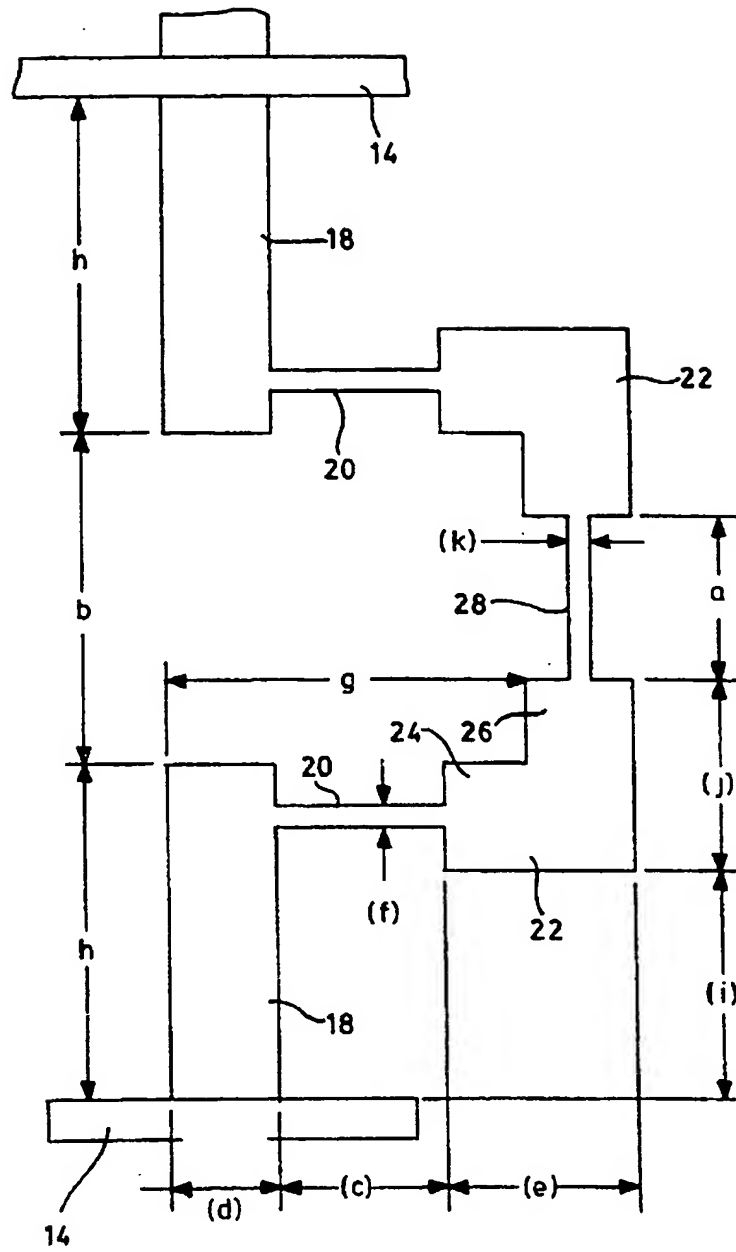


FIG. 4

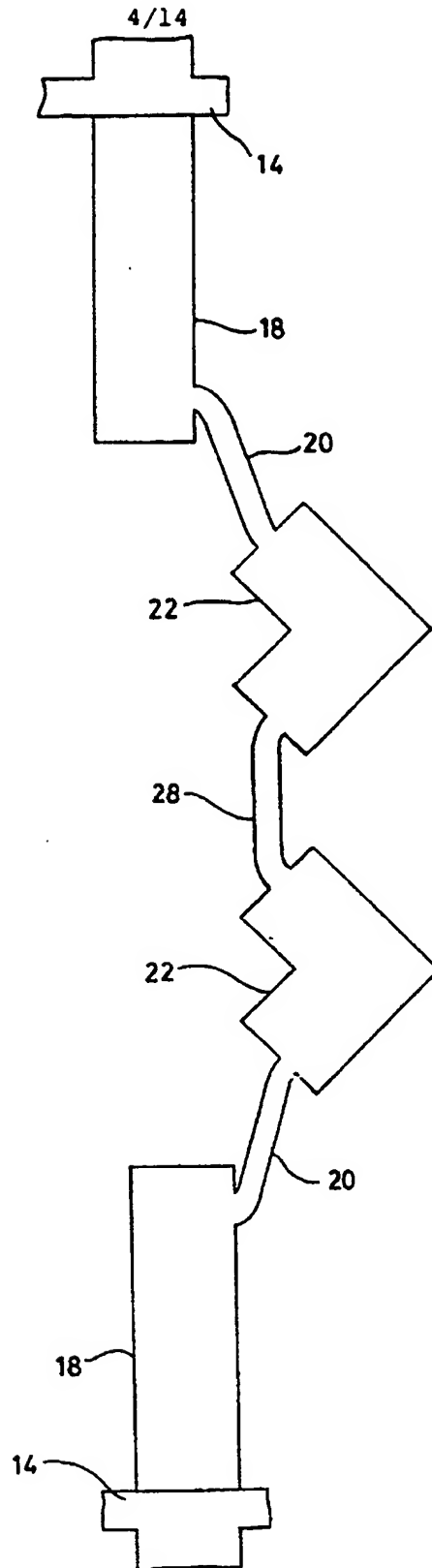
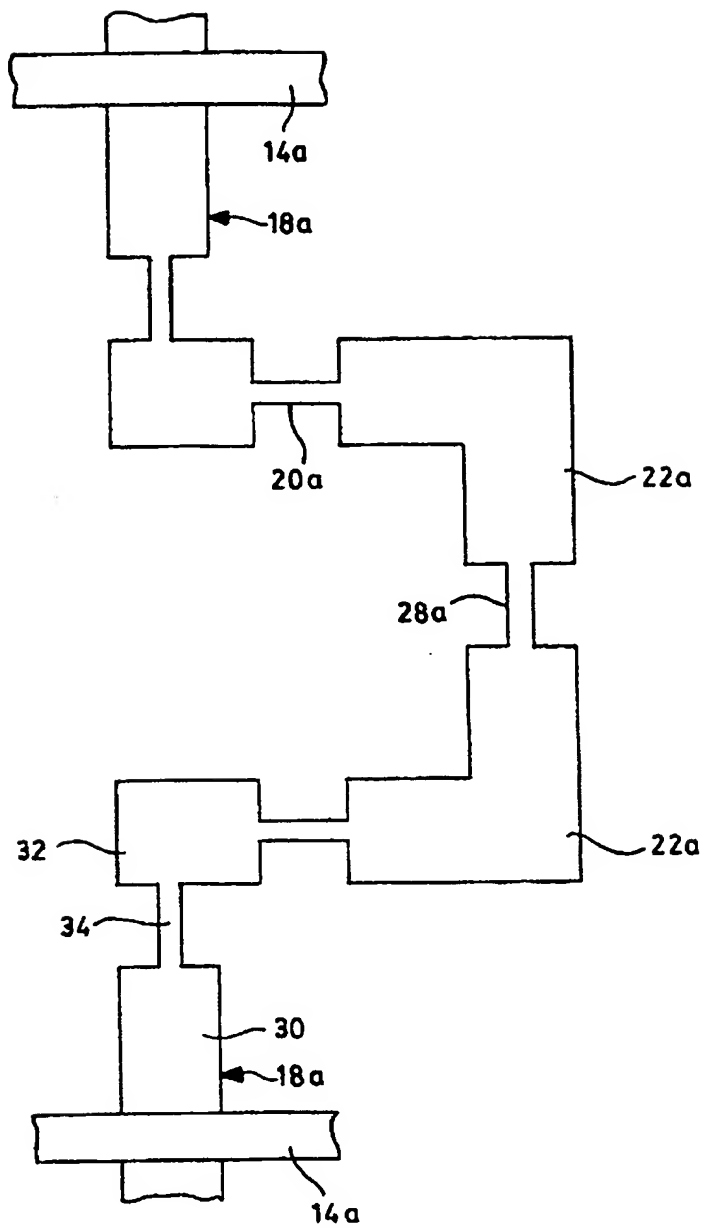


FIG. 5

5/14

FIG. 6

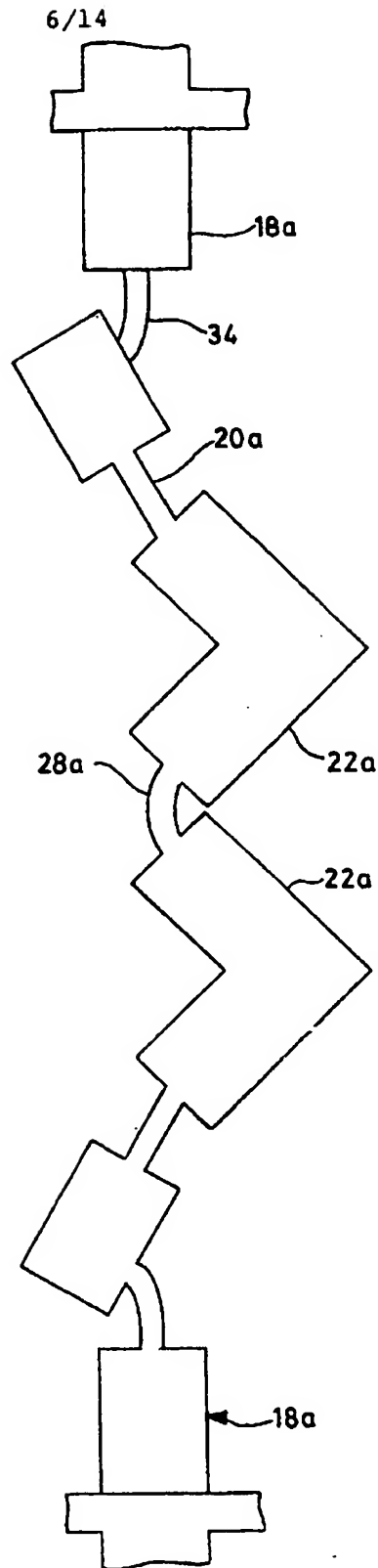


FIG. 7

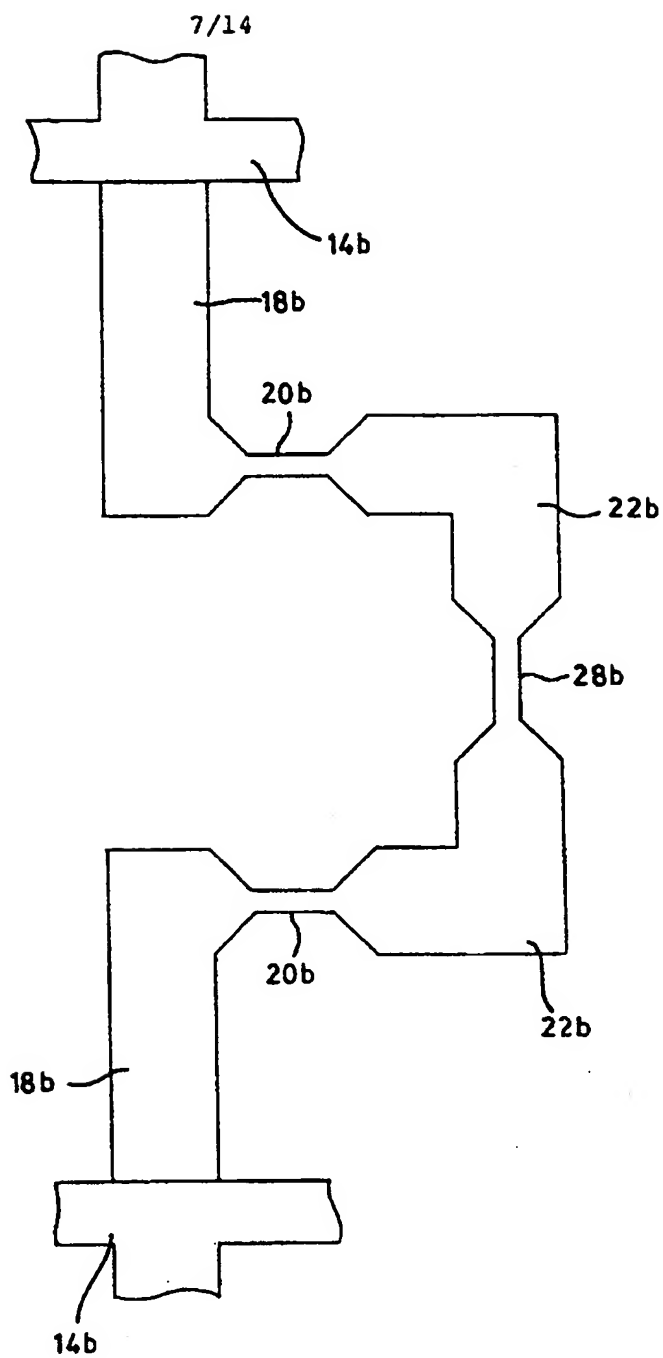
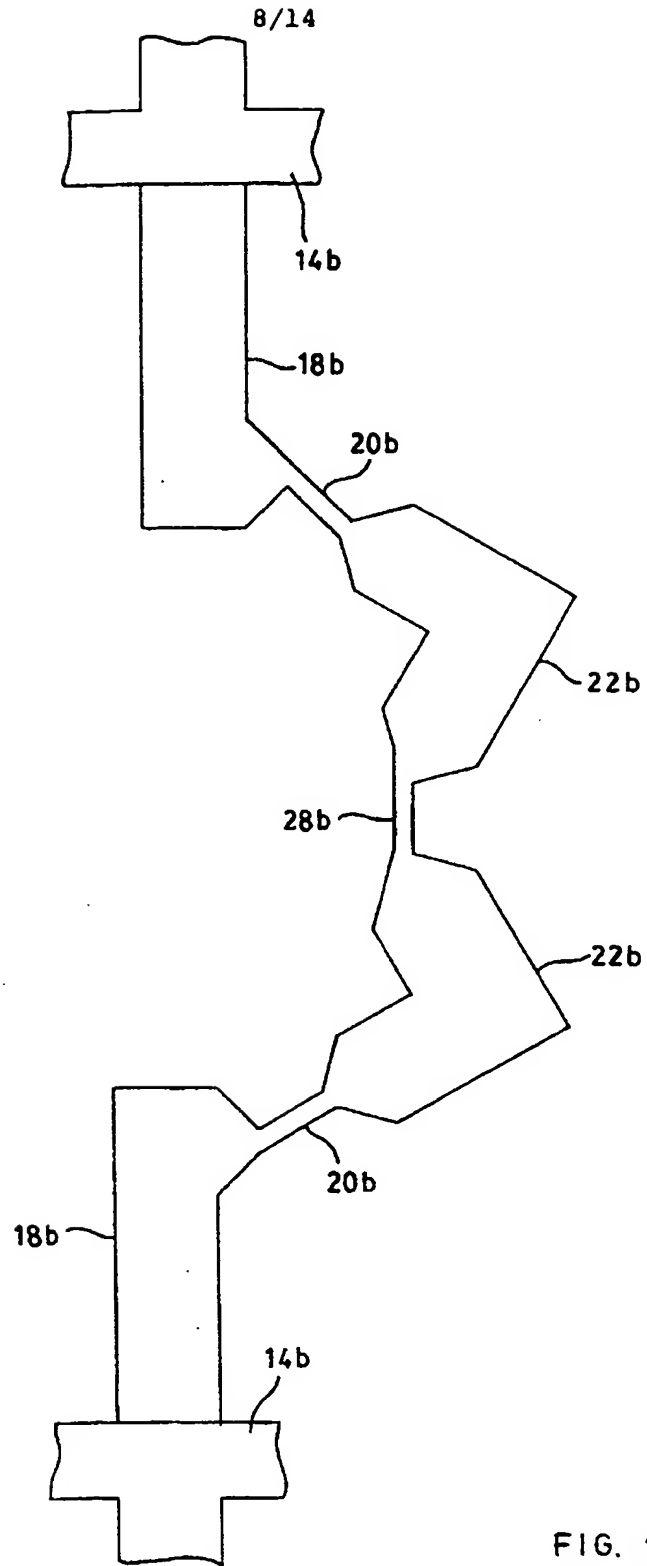
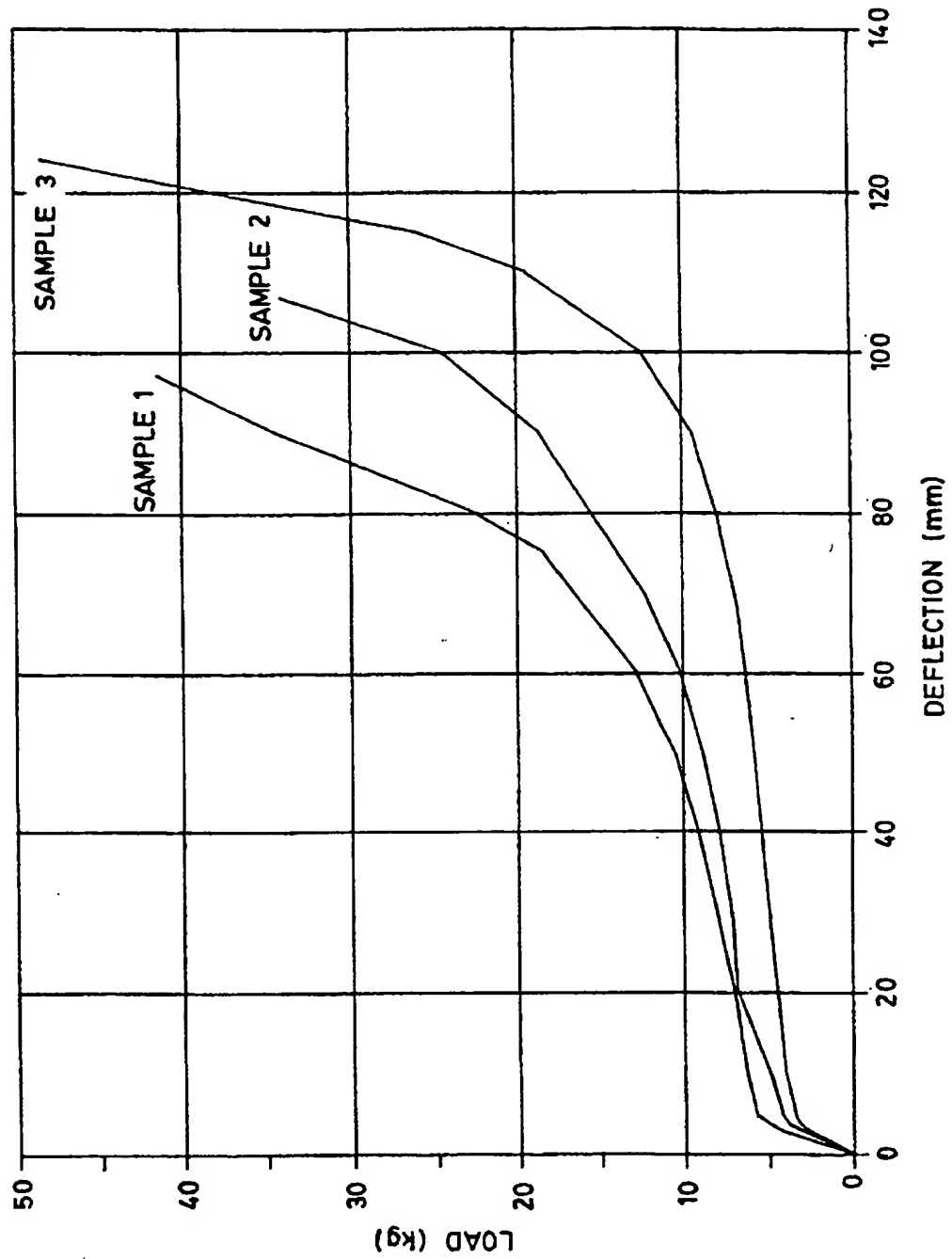


FIG. 8



9/14

FIG. 10

SUBSTITUTE SHEET (RULE 26)

10/14

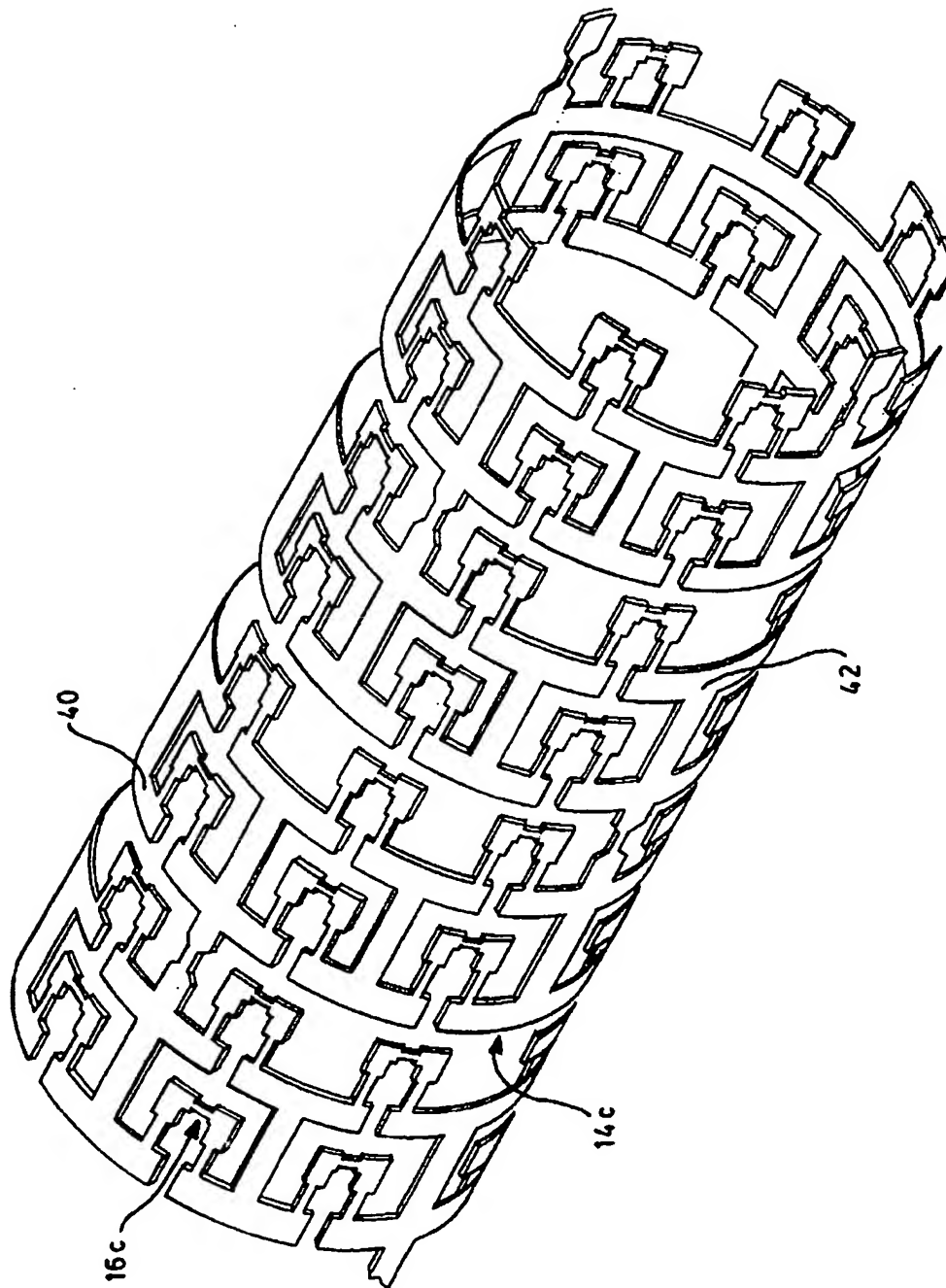
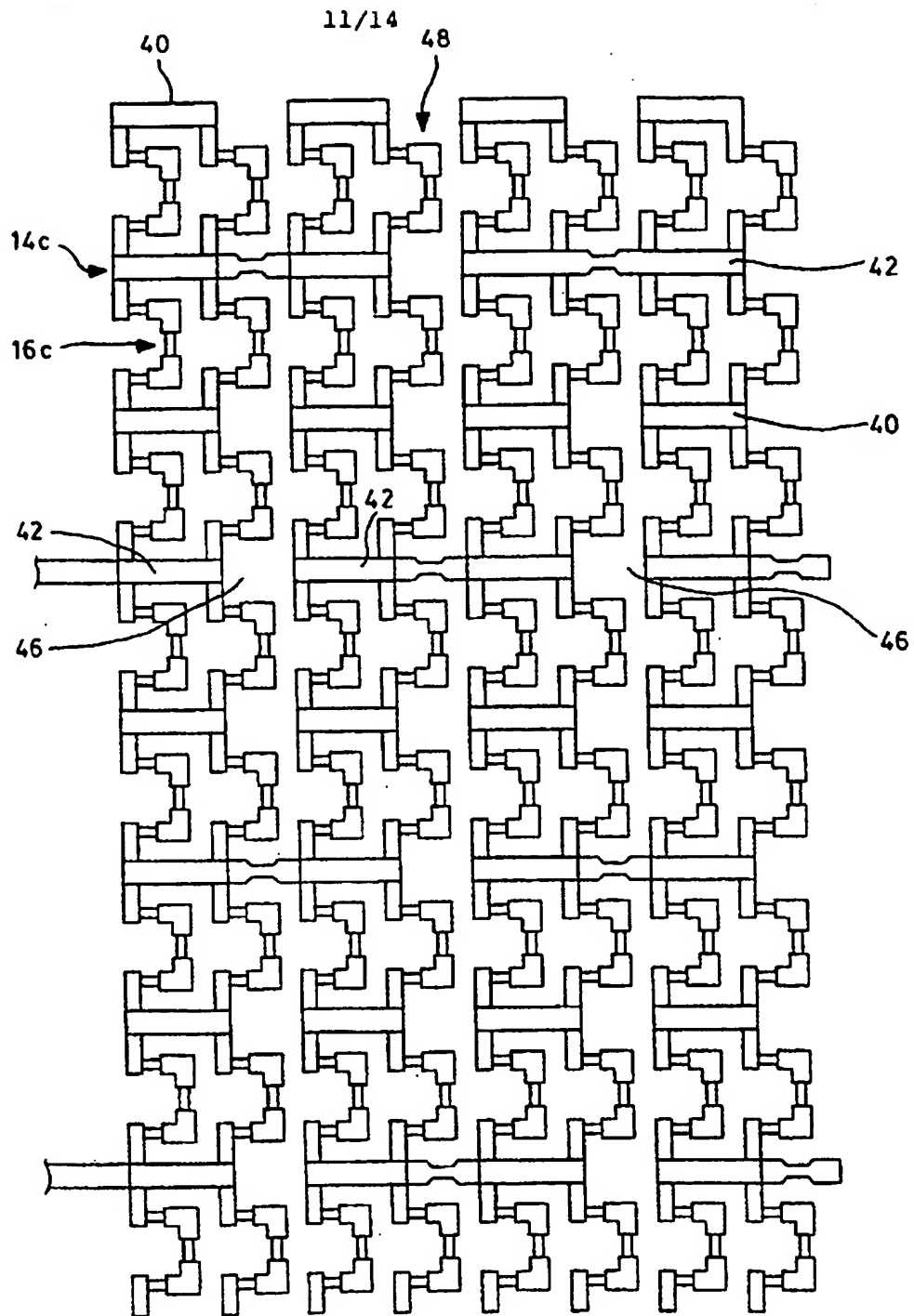


FIG. 11

FIG. 12

SUBSTITUTE SHEET (RULE 26)

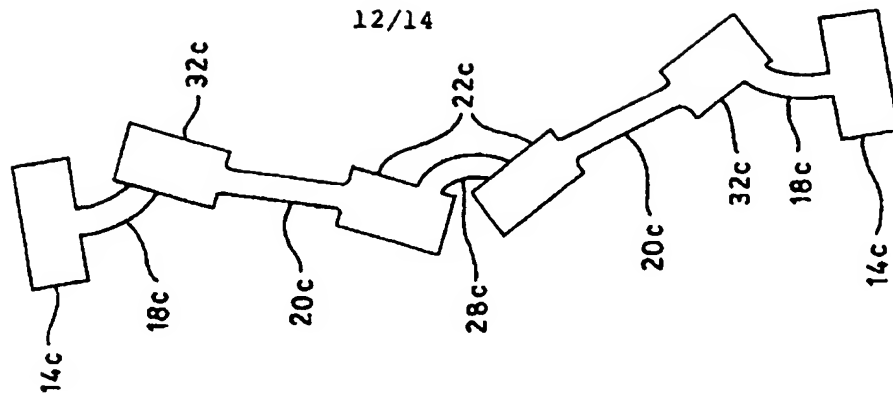


FIG. 14

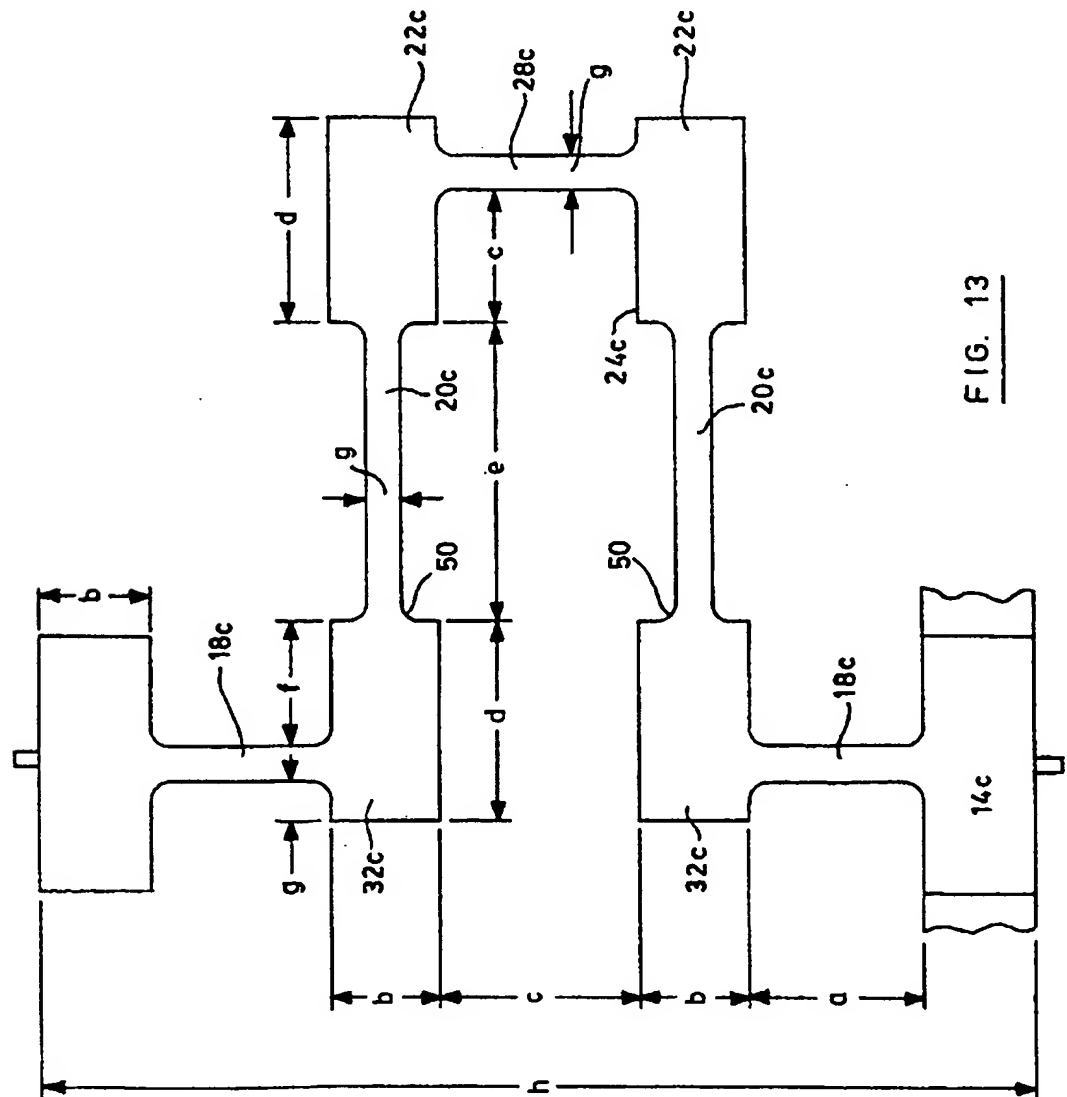


FIG. 13

13/14

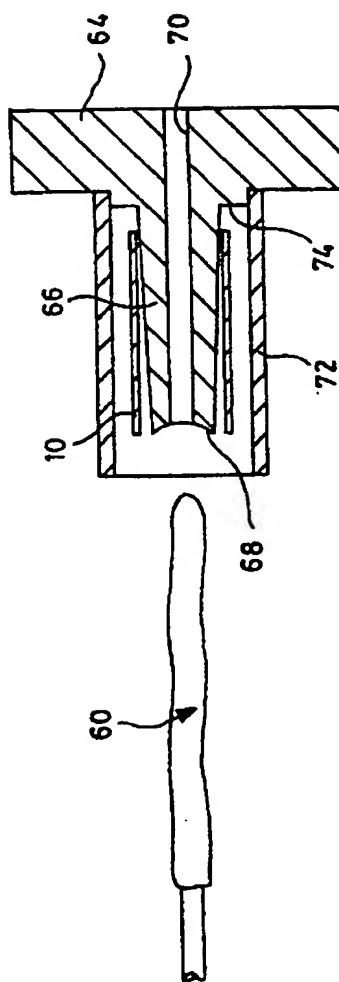


FIG. 15

14/14

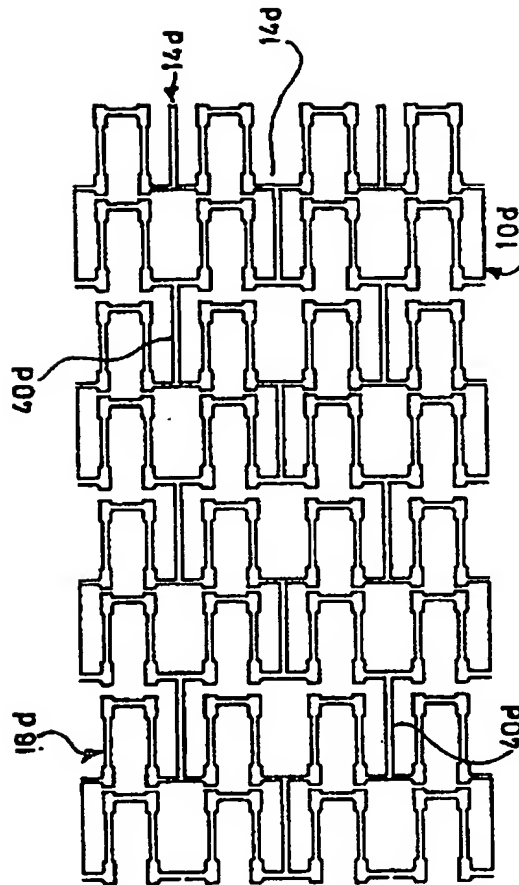


FIG. 16

INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA 96/00504

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61F2/06

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO,A,95 09584 (GUERBET SA ;BOUDGHENE FRANK (FR); MICHEL JEAN BAPTISTE (FR); SAPOV) 13 April 1995 see page 3, line 21 - line 34 see page 4, line 8 - line 11 see page 6, line 18 - line 26; figures 1-5	1,2,7,14
Y		8-11,15,16
A		3-6,12,13
Y	EP,A,0 540 290 (ADVANCED CARDEOVASCULAR SYSTEM) 5 May 1993 see column 5, line 57 - column 6, line 23; figures 4,5,7-10 --- -/-	8-11,15,16

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

Δ document member of the same patent family

Date of the actual completion of the international search

21 October 1996

Date of mailing of the international search report

24.10.96

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl,
Fax (+ 31-70) 340-3016

Authorized officer

Chabus, H

INTERNATIONAL SEARCH REPORT

International Application No
PCT/CA 96/00504

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	<p>WO,A,96 09013 (UNIV WAKE FOREST) 28 March 1996 see page 13, line 24 - line 28 see page 14, line 6 - line 13; figures 2,3,14 -----</p>	1,2,7,14

INTERNATIONAL SEARCH REPORT

Information on patent family members

Int. Application No

PCT/CA 96/00504

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO-A-9509584	13-04-95	FR-A- 2710834	14-04-95
		AU-A- 7858594	01-05-95
		CA-A- 2173500	13-04-95
		EP-A- 0722304	24-07-96
EP-A-0540290	05-05-93	CA-A- 2079417	29-04-93
		EP-A- 0734699	02-10-96
		JP-A- 6181993	05-07-94
		US-A- 5421955	06-06-95
		US-A- 5514154	07-05-96
WO-A-9609013	28-03-96	AU-A- 3418395	09-04-96